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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/448,356 | 11/23/1999 | DAVID CARL BURDICK | 20257/110665 | 4950 |

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| EXAMINER | |
|---|---|
| QAZI, SABIHA NAIM | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1616 | |

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/448,356 | BURDICK ET AL. | |
| | Examiner | Art Unit | |
| | Sabiha Qazi | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *3/3/05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4,8,24 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4,8,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## Final Office Action

Claims 1-4, 8, 24, and 25 are pending. No claim is allowed at present time. Applicant's response is hereby acknowledged.

## RESPONSE TO ARGUMENTS

Applicant's arguments were fully responded in our previous office action. All rejections are maintained. Applicants argue that presently claimed invention has a limitation of temperature from –20 to 20 C. It should be noted that claims are not drawn to process of making the compounds. Claims are drawn to compounds.

Applicant is requested to call the Examiner to discuss the issues surrounding the application.

## Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claim(s) 1-4, 8, 24 and 25 are rejected under 35 U.S.C. 103 as being unpatentable over Higgins, III (US Patent 6,147,236) and Higashidate et al. (J. of Chromatography, 515 (1990), 295-303). These references teach sterol esters and methyl esters of eicosapentaenoic ac id (EPA)

and docosahexaenoic acid (DHA), which embrace instantly, claimed invention. See the entire documents especially lines 9-67, col. 2; cols. 3 and 4; lines 1-20, col. 5 in US '236; see abstract and first Para on page 295, Table 1 and last two paragraphs on page 302 in Higashidate reference.

Instant claims differ from the reference in claiming nutritional supplement of specific sterol esters prepared by unsaturated fatty acid esters selected from EPA, DHA and Stearidonic acid (SA) whereas prior art US '236 teaches sterol esters with unsaturated fatty acids, examples given is same as one of the instantly claimed sterol ester i.e. sterol with DHA, sitosterol docosahexaenoate and sitostanol docosahexaenoate, see lines 13 and 14 in col. 5. Higashidate teaches DHA and EPA from fish oils and prevent diseases such as arteriosclerosis and myocardial infarction by lowering the concentration of lipids and cholesterol in blood. It discloses that fish oil is a rich source of such fatty acids. Stearidonic acid (SA) is also found in fish oil.

It would have obvious to one skill in the art to prepare additional beneficial nutritional supplement using sterols with a pendent ester functionality which when hydrolyzed provides another cholesterol-lowering agent. Since Higgins teaches such sterol esters and Higashidate teaches that fish oil contains omega-3 fatty acids (a class of PUFA) which includes docosahexaenoic acid (DHA) and eicosahexaenoic acid (EPA), one would find ample motivation to prepare sterol esters with unsaturated fatty acids from active compounds present in fish oil (known to be used as nutritional supplement to loer the cholesterol and triglyceride levels) or using unsaturated fatty acids from any other source for use as nutritional supplement.

2. Claim(s) 1-4, 8, 24 and 25are rejected under 35 U.S.C. 103 as being unpatentable over combined teachings of Mitchell (US 4,588,717) and Gregory J. Mishkel et al. (Bailliere's Clinical Haematology, Vol. 3, No. 3, July 1990, pp 625-649) and Kamarei et al. (US 4879,312). See the entire documents.

Mitchell (US Patent 4,588,717) teaches vitamin supplements containing phytosterol esters such as fatty acid esters of sterol, stigmasterol and taxasterol, in various combinations, a composition of the phytosterols, such as sitosterol, stigmasterorl, taraxasterol etc. reacted with polyunsaturated fatty acids such as linoleic acid, (18-carbons, two double bonds), linolenic acid (18-carbons, 3-double bonds), arachidonic acid (20-carbons, two double bonds). Fatty acid may have about 18-20 in addition to two carbon atoms of terminal carboxyl and methyl groups (lines 2-15, col. 6) and at least two double bonds such as arachidonic acid, linoleic acid and linolenic acids are used to make phytosterol esters, (see lines 21-58, col. 3; lines 43-65, col. 5; equation 1 and lines 1-11 in col. 8). Furthermore, it teaches that the reaction between any given phytosterol and any given fatty acid is essentially the same, and is characterized in equation 1 using sitosterol and linoleic acid as an exemplary fatty acid.

Mishkel et al. teaches that fish oil containing omega-3 fatty acids lower the serum and cholesterol levels, and their beneficial effect on preventing and treating cardiovascular disease. See 1st Para on page 626, third paragraph on page 629, second Para on page 628. Specific use of DHA and EPA as dietary supplement are disclosed on section "Angina" on page 634.

Kamarei et al. teach that a diet rich in omega-3-fatty acids has beneficial effects in humans, including a reduction in plasma cholesterol and triglyceride levels, improved fat tolerance, prolonged bleeding time reduce platelet counts and decreased platelet adhesiveness.

The omega-3-fatty acids are obtained mainly from dietary seafood. It teach n-3 Poly unsaturated fatty acids (PUFA) participation and reasons why these materials may be involved in alleviating ischemic heart diseases. Furthermore, it also teaches that one of n-3 PUFA i.e. eicosapentaenoic acid (EPA) and DHA reduces triglyceride and very low-density lipoprotein (VLDL) serum levels and reduces whole blood viscosity. (See lines 39-59, col. 2; lines 13-54, col. 3; Table 1 and 2 in col. 4).

Instant claims differ from the reference in claiming nutritional supplement of phytosterol ester with specific fatty acids i.e. docosahexaenoic acid, stearidonic acid and eicosahexaenoic acid where US '717 teaches phytosterol ester with fatty acids especially containing poly unsaturated fatty acid approximately 2-22 carbon atoms. See examples 51-75 in col. 6, equation 2 in cols 15, 16, 17 and 18. Mishkel et al. teaches that polyunsaturated fatty acids from fish oil is used to preventing and treating cardiovascular disease. Furthermore, it teaches two major biologically active fish oil compounds, EPA and DHA.

Note, that Kamarie that n-3 PUFA i.e. eicosapentaenoic acid (EPA) and DHA reduces triglyceride and very low-density lipoprotein (VLDL) serum levels and reduces whole blood viscosity. (See lines 39-59, col. 2; lines 13-54, col. 3 and Table 1 and 2 in col. 4).

It would have been obvious to one skilled in the art to prepare additional beneficial nutritional supplement using sterols with a pendent ester functionality which when hydrolyzed provides another cholesterol-lowering agent. Since Mishkel teaches that fish oil contains omega-3 fatty acids (a class of PUFA) which includes docosahexaenoic acid (DHA) and eicosahexaenoic acid (EPA), see especially last para on page 625 of Mishkel reference). There has been ample motivation provided by the prior art to prepare the instant invention.

**Conclusion**

Since US' 236 teaches food grade sitosterol docosahexaenoate and sitostanol docosahexaenoate and other references cited above teach DHA , EPA and fish oil containing n-3 PUFA i.e. eicosapentaenoic acid (EPA) and DHA reduces triglyceride and very low-density lipoprotein (VLDL) serum levels and reduces whole blood viscosity, instant invention is considered obvious for the reasons cited above.

The compounds and compositions as claimed in present invention are considered obvious for the reasons as cited above.

Examiner notes the limitation of temperature (-20C to 20C) in claim 1.

Normally, change in temperature, concentration, or both, is not a patentable modification; however, such changes may impart patentability to a process if the ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from results of prior art; such ranges are termed "critical" ranges, and applicant has burden of proving such criticality; even though applicant's modification results in great improvement and utility over prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art; more particularly, where the general conditions of the claim are disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation. In re Aller et al. 105 USPQ 233.

It is well established that merely selecting proportions and ranges is not patentable absent a showing of criticality. In re Becket, 33 U.S.P.Q. 33 (C.C.P.A. 1937). In re Russell, 439 F.2d 1228, 169 U.S.P.Q. 426 (C.C.P.A. 1971).

It is a general rule that merely discovering and claiming a new benefit of an *old* process cannot render the process again patentable. Nor can patentability be found in differences in ranges recited in the claims. When the difference between the claimed invention and the prior

art is some range or other variable within the claims, the applicant must show that the particular range is *critical*, generally by showing that the claimed range achieves unexpected results relative to the prior art range. In re Woodruff, 16 USPQ2d 1934.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

## Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day.

Fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER